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L3: Entry 28 of 32 File: USPT Feb 18, 1997

DOCUMENT-IDENTIFIER: US 5603872 A
**** See image for Certificate of Correction ****
TITLE: Method of binding recognizing substances to liposomes

Drawing Description Text (2):
FIG. 1 shows the binding of bioadhesive liposomes (EGF-modified; open double triangle) and regular liposomes (asterisk) of the LUVET type to A431 cells in culture (in monolayers), as dependent upon liposome concentration. Bound liposomes, denoted as B, are in units of ng EGF per 10.sup.6 cells. Free ligand concentration, denoted as L, are in units of ng EGF per 10.sup.6 cells for bioadhesive liposome (first row of L values) and in units of umoles lipid per 10.sup.6 cells for the regular liposomes (second row of L values).

Detailed Description Text (12):
The "level of covalent binding" as reported in the Examples below is defined as the quantity of bioadhesive ligand, such as collagen, gelatin, hyaluronic acid or EGF bound to a given quantity of lipid in the final product since the most accurate quantitative measure of liposomes is in terms of lipid quantities. For a given lipid quantity, different liposome types will yield different quantities of liposome. Therefore, similar initial ratios of EGF to lipid for different liposome types should not be expected to yield the same level of binding. Another factor which would yield different results for different liposomes even under the same initial EGF to lipid ratios, is the differences in particle size, therefore in curvature, number and accessibility of PE sites on the surface of the liposome. Therefore, comparisons among liposome types should be avoided.

Current US Cross Reference Classification (3):
424/450

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L3: Entry 26 of 32 File: USPT Aug 18, 1998

DOCUMENT-IDENTIFIER: US 5795587 A
**** See image for Certificate of Correction ****
TITLE: Stable lipid-comprising drug delivery complexes and methods for their production

Detailed Description Text (24):
In the cationic liposomes utilized to produce the drug/lipid complexes of this invention, the cationic lipid is present in the liposome at from about 10 to about 100 mole % of total liposomal lipid, preferably from about 20 to about 80 mole % and most preferably about 20 to about 60 mole %. The neutral lipid, when included in the liposome, may be present at a concentration of from about 0 to about 90 mole % of the total liposomal lipid, preferably from about 20 to about 80 mole %, and most preferably from 40 to 80 mole %. The negatively charged lipid, when included in the liposome, may be present at a concentration ranging from about 0 mole % to about 49 mole % of the total liposomal lipid, preferably from about 0 mole % to about 40 mole %. In a preferred embodiment, the liposomes contain a cationic and a neutral lipid, most preferably DC-Chol and DOPE in ratios between about 2:8 to about 6:4. It is further understood that the complexes of the present invention may contain modified lipids, protein, polycations or receptor ligands which function as a targeting factor directing the complex to a particular tissue or cell type. Examples of targeting factors include, but are not limited to, asialoglycoprotein, insulin, low density lipoprotein (LDL), folate and monoclonal and polyclonal antibodies directed against cell surface molecules. Potential targets include, but are not limited to, liver, blood cells, endothelial cells and tumor cells.

Current US Original Classification (1):
424/450

L3: Entry 22 of 32 File: USPT Nov 16, 1999

US-PAT-NO: 5985852
DOCUMENT-IDENTIFIER: US 5985852 A

TITLE: Inhibition of selectin binding

DATE-ISSUED: November 16, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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US-CL-CURRENT: 514/54; 424/450, 514/23, 514/25, 514/53, 514/61, 514/62, 536/1.11, 536/17.2, 536/18.7, 536/4.1, 536/53, 536/55, 536/55.1, 536/55.2

CLAIMS:

What is claimed as the invention is:

1. A composition for inhibiting binding between a first cell having a P- or L-selectin and a second cell having a ligand for the selectin, comprising a sheet of lipids wherein a proportion of the lipids sufficient to stabilize the sheet are covalently crosslinked, a proportion of the lipids have an attached saccharide which meets the carbohydrate binding requirements of selectins, and a proportion of the lipids not having an attached saccharide have an acid group that is negetively charged at neutral pH which meets the anionic binding requirement of P- and L-selectin.

2. The composition of claim 1, wherein the saccharide is a sialylated fucooligosaccharide or analog thereof.

3. The composition of claim 1, wherein the saccharide is a sulfated fucoohgosaocharide.

4. The composition of claim 1 wherein the attached saccharide is a neutral saccharide.

5. The composition of claim 1, wherein the saccharide is selected from the group consisting of lactose and maltose.

6. The composition of claim 1 wherein the attached sacdiaride is a disaccharide.

7. The composition of claim 1 wherein a proportion of the lipids having an attached saccharide are covalently crosslinked to other lipids in the sheet.

8. The composition of claim 1 wherein a proportion of lipids having an attached saccharide are not covalenty crosslinked to other lipids in the sheet.

9. The composition of claim 1, wherein a proportion of the lipids in the lipid sheet have a first attached saccharide, and a separate proportion of the lipids in the lipid sheet have a second attached saccharide that is different from the first.

10. The composition of claim 1, wherein the first attached saccharide is fucose and the second attached saccharide is a sulfated or acidic monosaccharide.

11. The composition of claim 1, wherein the acid group is a carboxylic acid.

12. The composition of claim 1, wherein the acid group is a negatively charged sulfate or phosphate group.

13. The composition of claim 1, wherein the lipid sheet is part of the lipid bilayer of a liposome.

14. The composition of claim 1, wherein the lipids each contain a single aliphatic hydrocarbon.

15. The composition of claim 1, wherein the composition inhibits binding of the ligand to the selectin.

16. The composition of claim 1, wherein the composition has a 50% inhibition concentration (IC.sub.50) that is 10.sup.2 -fold lower than that of monomer sLe.sup.x.

17. The composition of claim 1, wherein the composition has a 50% inhibition concentration (IC.sub.50) that is 10.sup.4 -fold lower than that of monomer sLe.sup.x.

18. The composition of claim 1, wherein the composition has an IC.sub.50 in a selectin-to-cell binding assay of less than 100 nM.

19. The composition of claim 1, wherein the selectin is P-selectin.

20. The composition of claim 1, wherein the selectin is L-selectin.

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L3: Entry 32 of 32 File: USPT Apr 3, 1990

DOCUMENT-IDENTIFIER: US 4913902 A
TITLE: Purification by affinity binding to liposomes

Brief Summary Text (13):
Ligands which will bind to any of a variety of target molecules can be bound to liposomes to practice the present invention. Exemplary of such ligands, and the target molecules bound thereby, are the following: Biotin and Avidin; Monoclonal Antibodies and Inhibin; Procainamide and Cholinesterase; N-methyl Acridinium and Acetylcholinesterase; P-aminobenzamidine and Trysin; P-aminophenol-beta-D-thiogalacto-pyranoside and Beta-Galactosidase; Chitin and Lysozyme; Methotrexate and Dihydrofolate Reductase; AND and Alcohol Dehydrogenase; Sulfanilamide and Carbonic Anhydrase; DNA and DNA Polymerase; DNA and cDNA; DNA and RNA; cDNA and Genetically Engineered Plasmids; Oxidized Glutathione and Glutathione Reductase; P-aminobenzamidine and Urokinase; Monoclonal Antibodies and Insulin; Trypsin and Soybean Trypsin Inhibitor; N.sup.6 -aminocaproyl-3',5'-cAMP and Protein Kinase; Pepstatin and Renin; 4-Chlorobenzylamine and Thrombin; Monoclonal Antibodies and Interferon; N-(4-amino phenyl) Oxamic Acid and Influenza Virus; Prealbumin and Retinal-binding Protein; Neurophysin and Vasopressin; Lysine and Plasminogen; Heparin and Antithrombin; Cycloheptaamylose and Human Serum Amylase; Cortisol and Transcortin; Pyridoxal-5-phosphate and Glutamate-pyruvate transaminase; Chelating Agents and Metal Ions; Chelating Agent-Cu and Superoxide Dismutase; Chelating Agent-Zn and Human Fibrinogen; Coenzyme A and Succinic Thiokinase; Flavin and Luciferase; Pyridoxal Phosphate and Tyrosine Aminotransferase; Porphyrin and Haemopexin; Lysine and Ribosomal RNA; Polyuridine and mRNA; Concanavalin A and Immunoglobulins; 3-phospho-3hydroxypropionate and Enolase; D-malate and Fumarate Hydratase; Atropine or Cobratoxin and Cholinergic Receptors; 6-Aminopenicillanic acid and D-Alanine Carboxypeptidase; Plant Lectins and Epidermal Growth Factor Receptors; Alprenolol and Epinephrine Receptors; Growth Hormone and Prolactin Receptors; Insulin and Insulin Receptors; Estradiol or Diethylstilbestrol and Estrogen Receptors; Dexamethasone and Glucocorticoid Receptors; Hydroxycholecalciferol and Vitamin D Receptors; Virus Monoclonal Antibodies and Blood Viruses; and Monoclonal Antibodies and Bacteriophages. Suitable chelating agents for practicing the present invention include ethylenediaminetetraacetic acid (EDTA) and other compounds containing the iminodiacetic acid group, phosphonoacetic acid (H.sub.2 O.sub.3 P-CH.sub.2 COOH), pyrophosphate (such as dibasic pyrophosphate hexahydrate), dibasic orthophosphate, crown ethers such as dicyclohexano-18-crown-6, cyclodextrins, cryptands. In overview, suitable ligands include, but are not limited to, antibodies, peptides, polynucleic acids, antitoxins, chelating agents, enzyme inhibitors, receptor agonists, and receptor antagonists. The term "antibody," as used herein, means immunoglobulins such as IgA, IgG, IgM, IgD, and IgE, whether polyclonal or monoclonal in origin. These ligands may be covalently bound to phospholipids used to form liposomes by conventional techniques, either by attaching the ligand to preformed liposomes or by binding the ligand to a phospholipid and incorporating the resulting amphiphilic molecules into liposomes during formation thereof. For example, liposomes with antibodies linked thereto may be produced in the manner disclosed in U.S. Pat. No. 4,483,929 to Szoka.